IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 5974**
Hidenobu YAKU et al.	:	Attorney Docket No. 2003_1763A
Serial No. 10/727,664	:	Group Art Unit 1634
Filed December 5, 2003	:	Examiner Thomas J. O'Farrell
METHOD, PRIMER AND KIT FOR DETERMINING BASE TYPE	:	Mail Stop: **Amendment**

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Hidenobu YAKU, the undersigned, a citizen of Japan, residing at 7-1-202, Ishizuminamimachi, Neyagawa-shi, Osaka 572-0024, Japan, do hereby declare:

1. That I am an inventor of the above-identified application.

2. That I graduated from Graduate School of Nagoya University on March 31, 1999 with a degree in Bioagricultural Sciences.

3. That I currently work as a researcher at Matsushita Electric Industrial Co., Ltd located at 1006, Oaza Kadoma, Kadoma-shi, Osaka 571-8501 Japan.

4. That I have read the specification and claims of the above-identified application. I have also read the Office Action dated February 15, 2006, including the following 103(a) obviousness rejections and the references cited therein:

(1) the rejection of claims 1-6, 9, 20 and 21 under 35 U.S.C. § 103(a) as obvious over Sorenson;

(2) the rejection of claims 7 and 8 under 35 U.S.C. § 103(a) as obvious over Sorenson in view of Kambara;

(3) the rejection of claim 22 under 35 U.S.C. § 103(a) as obvious over Sorenson in view of Newton (US 5,525,494); and

(4) the rejection of claims 14-19 under 35 U.S.C. § 103(a) as obvious over Sorenson in view of Kambara and Bille et al. (Phys. Plantarun, Vol. 84, pp. 250-254 (1992)).

5. That in order to show the novelty and unobviousness of the claimed base type determination method for determining a base type of a monobasic substituted region of a target nucleic acid of the above-identified application, I have under my control and direction conducted supplementary experiments (First Experiment - Fifth Experiment), the particulars and results of which are attached herewith.

The prior art teaching of Sorenson was relied upon as teaching (at page 16, lines 1-3) that allele specific primers can have some mismatches 3-6 nucleotides from a 3' end that would not be likely to interfere with efficacy (of SNP detection).

The results of the attached experiments (First Experiment - Fifth Experiment) show a clear difference between the allele-specific primers according to the present invention and those in the prior art. In particular, the results show that the allele-specific primers according to the present invention achieve a significantly superior pseudo-positive repression effect over the prior art allele specific primers as represented by Sorenson.

In Figs. 1-5 of the supplementary experimental data attached herewith, each of the vertical scales represents "a concentration of amplified products" or "a ratio of fluorescence intensity", which indicates occurrence of an incorrect determination of a base in a substituted region (i.e., a determination of pseudo-positive). In other words, the higher the concentration of amplified products or the ratio of fluorescence intensity is, the greater the determination of incorrect pseudo-positives.

In the attached experiments, the following samples correspond to the prior art primers:

Samples (1-1) to (1-3) in the First Experiment (paragraph bridging pages 1-2),
Samples (2-1) to (2-3) in the Second Experiment (last paragraph on page 5),

Samples (3-1) to (3-3) in the Third Experiment (paragraph bridging pages 9-10),
Samples (4-1) to (4-3) in the Fourth Experiment (paragraph bridging pages 13-14), and
Samples (5-1) to (5-3) in the Fourth Experiment (page 18).

In the attached experiments, the following samples correspond to the allele-specific primers according to the present invention:

Samples (1-4) to (1-8) in the First Experiment (paragraph bridging pages 1-2),
Samples (2-4) to (2-8) in the Second Experiment (last paragraph on page 5),
Samples (3-4) to (3-8) in the Third Experiment (paragraph bridging pages 9-10),
Samples (4-4) to (4-8) in the Fourth Experiment (paragraph bridging pages 13-14), and
Samples (5-4) to (5-8) in the Fourth Experiment (page 18).

The results of these experiments show that when a base in the second position from 3' terminal end of the primer is complementary to a target nucleic acid, as in samples (1-1) to (1-3), (2-1) to (2-3), (3-1) to (3-3), (4-1) to (4-3) and (5-1) to (5-3) (as in the prior art), the concentration of amplified products is equal to or greater than 100nM and the ratio of fluorescence intensity is equal to or greater than 50%.

In contrast, if a base in the second position from 3' terminal of the primer is uncomplementary to a target sequence, as shown in samples (1-4) to (1-8), (2-4) to (2-8), (3-4) to (3-8), (4-4) to (4-8) and (5-4) to (5-8) (as in the present invention), the concentration of amplified products and the ratio of fluorescence intensity are substantially zero.

The data in the attached experiments clearly show that the use of the prior art allele specific primers produce false positives, whereas the allele specific primers of the present invention significantly reduce false positives.

6. Based on the results of these experiments, it is my position that the allele specific of the present invention achieve a significantly superior pseudo-positive repression effect over the prior art allele specific primers as represented by Sorenson, and the present invention is novel and unobviousness over the prior art references cited in the Office Action.

7. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Date: June 21, 2006

Hidenobu YAKU

Hidenobu YAKU